MT-TH Gene

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mitochondrially encoded tRNA histidine

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1. Introduction

The *MT-TH* gene provides instructions for making a particular type of RNA, a molecule that is a chemical cousin of DNA. This type of RNA, called transfer RNA (tRNA), helps assemble protein building blocks known as amino acids into full-length, functioning proteins. The *MT-TH* gene provides instructions for a specific form of tRNA that is designated as $tRNA^{His}$. During protein assembly, this molecule attaches to a particular amino acid, histidine (His), and inserts it into the appropriate locations in the growing protein.

The $tRNA^{His}$ molecule is present in cellular structures called mitochondria. These structures convert energy from food into a form that cells can use. Through a process called oxidative phosphorylation, mitochondria use oxygen, simple sugars, and fatty acids to create adenosine triphosphate (ATP), the cell's main energy source. The $tRNA^{His}$ molecule is involved in the assembly of proteins that carry out oxidative phosphorylation.

2. Health Conditions Related to Genetic Changes

2.1. Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes

A small number of people with the features of mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) have a mutation in the *MT-TH* gene. This condition is characterized by recurrent severe headaches, muscle weakness (myopathy), hearing loss, stroke-like episodes including a loss of consciousness, seizures, and other problems affecting the nervous system. Some people with an *MT-TH* gene mutation also have features of another mitochondrial disorder called myoclonic epilepsy with ragged-red fibers (MERRF); these additional features can include muscle twitches (myoclonus), difficulty coordinating movement (ataxia), and abnormal muscle cells known as ragged-red fibers. This combination of signs and symptoms is called MERRF/MELAS overlap syndrome.

MT-TH gene mutations that cause MELAS and MERRF/MELAS overlap syndrome change single DNA building blocks (nucleotides) in the gene. Researchers have not determined how these genetic changes alter energy production in mitochondria or cause the varied signs and symptoms of MELAS or MERRF/MELAS overlap syndrome.

2.2. Myoclonic epilepsy with ragged-red fibers

As mentioned above, a few individuals with a mutation in the *MT-TH* gene have features of both myoclonic epilepsy with ragged-red fibers (MERRF) and MELAS. The mutation involved in this overlap syndrome replaces the nucleotide guanine with the nucleotide adenine at gene position 12147 (written as G12147A). It remains unknown why this mutation causes the overlapping features of MERRF and MELAS.

2.3. Other disorders

Another mutation in the *MT-TH* gene may increase the risk of developing a heart condition called cardiomyopathy. People with cardiomyopathy have a weakened heart muscle that is unable to pump blood effectively. A particular change in the *MT-TH* gene has been identified in several adults with cardiomyopathy, but without other common signs of mitochondrial disease such as neurological abnormalities. This mutation replaces the nucleotide guanine with the nucleotide adenine at gene position 12192 (written as G12192A). It is unclear why this alteration in mitochondrial DNA may increase a person's risk of developing heart problems without affecting other parts of the body.

3. Other Names for This Gene

- MTTH
- tRNA histidine

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